

Table 1. Mechanism of Absorption in the Small Intestine

BCS Class III Drugs	Active Membrane Transporters						Paracellular Diffusion
	Influx Transporters			Efflux Transporters			
	PEPTs	OATPs	OCTs	P-gp	BCRP	MRP2	
Ranitidine	× ^{[1][2][3]}	× ^{[1][2][3]}	√ ^[4]	√ ^{[5][6]}	× ^[6]	× ^[6]	√ ^[6]
Ampicillin	√ ^[5]		× ^{[1][7][8]}	√ ^[9]			√ ^[10]
Metformin	× ^{[1][2][3]}	× ^{[1][2][3]}	√ ^[11]	× ^[12]	× ^[1]		√ ^[13]

√ stands for the substrates. × stands for this drug is neither inhibitor nor substrates for the transporter.

^[1](Konig et al., 2013) ^[2](Leibach and Ganapathy, 1996) ^[3](Liang et al., 1995) ^[4](Muller et al., 2005) ^[5](Bourdet et al., 2006) ^[6](Collett et al., 1999) ^[7](Muller et al., 2012) ^[8](Tsuji et al., 1981) ^[9](Siarheyeva et al., 2006) ^[10](Lafforgue et al., 2008) ^[11](Chen et al., 2010) ^[12](Song et al., 2006) ^[13](Alvi and Chatterjee, 2014)

Table 2. Chromatographic conditions and parameters for quantification of ampicillin, metformin and ranitidine in rat plasma.

Model Drugs	Column	Column Temperature (°C)	Wavelength (nm)	Mobile Phase	Flow Rate (mL/min)	Injection Volume (µL)	Reference
Ampicillin	C18 (250mm×4.6mm I.D./5µm)	25	220	10mM Sodium Dihydrogen Phosphate Buffer(pH 7.0, 60%); Methanol(40%)	0.6	50	This paper
Metformin	C18 (250mm×4.6mm I.D./5µm)	25	234	10mM Sodium Dihydrogen Phosphate Buffer with 10mM Sodium Dodecyl Sulfonate(pH 7.0, 60%); Acetonitrile(40%)	1	50	This paper
Ranitidine	SCX (250mm×4.6mm I.D./5µm)	50	320	0.1M Sodium Acetate Buffer(pH 5.0, 80%); Acetonitrile(20%)	2	40	(Ashiru et al., 2008)

Table 3. Effect of PEG 400 on the pharmacokinetic parameters of ampicillin in male and female Wistar rats (Mean±S.D.,n=6). * Values are statistically different between the control and PEG groups at p<0.05.

Pharmacokinetic Parameters	Male		Female	
	Control	26mg/kg PEG 400	Control	26mg/kg PEG 400
AUC ₀₋₄₈₀ (µg.min/mL)	528 ± 52	807 ± 30 *	640 ± 43	687 ± 28
AUC _∞ (µg.min/mL)	577 ± 74	939 ± 58 *	734 ± 31	897 ± 72
c _{max} (µg/mL)	3 ± 0.3	5 ± 0.7 *	3 ± 0.6	3 ± 0.2
t _{max} (min)	109 ± 23	38 ± 18 *	123 ± 33	144 ± 33
CL (mL/min)	0.02 ± 0.003	0.01 ± 0.0008	0.02 ± 0.0007	0.01 ± 0.003
Vd (mL)	5 ± 1	3 ± 0.4	4 ± 0.7	5 ± 2
t _{1/2} (min)	156 ± 43	161 ± 27	148 ± 28	210 ± 34

Table 4. Effect of PEG 400 on the pharmacokinetic parameters of metformin in male and female Wistar rats (Mean±S.D.,n=6). * Values are statistically different between the control and PEG groups at p<0.05.

Pharmacokinetic Parameters	Male		Female	
	Control	26mg/kg PEG 400	Control	26mg/kg PEG 400
AUC ₀₋₄₈₀ (µg.min/mL)	126 ± 12	114 ± 19	119 ± 12	121 ± 13
AUC _∞ (µg.min/mL)	130 ± 12	117 ± 20	129 ± 14	125 ± 14
c _{max} (µg/mL)	0.6 ± 0.1	0.5 ± 0.1	0.5 ± 0.06	0.5 ± 0.07
t _{max} (min)	98 ± 25	125 ± 47	135 ± 59	75 ± 32
CL (mL/min)	0.09 ± 0.008	0.1 ± 0.02	0.1 ± 0.01	0.1 ± 0.01
Vd (mL)	13 ± 2	19 ± 6	18 ± 3	15 ± 4
t _{1/2} (min)	100 ± 15	119 ± 23	129 ± 18	102 ± 14

Table 5. Effect of CsA on the pharmacokinetic parameters of ampicillin, ranitidine and metformin in male and female Wistar rats (mean±standard deviation, n=5). * Values are statistically different between the control and CsA groups at p<0.05.

Pharmacokinetic Parameters	Male		Female	
	Control	50mg/kg CsA	Control	50mg/kg CsA
Ampicillin				
AUC ₀₋₄₈₀ (µg.min/mL)	528±52	1209±186 *	640±43	892±89 *
AUC _∞ (µg.min/mL)	577±74	1287±185 *	734±31	1003±57 *
c _{max} (µg/mL)	3±0.3	6±1 *	3±0.6	4±1
t _{max} (min)	109±23	105±56	122±33	123±37
CL (mL/min)	0.02±0.003	0.01±0.001	0.02±0.0007	0.013±0.0008
Vd (mL)	5±1	2±0.4	4±0.7	4±1
t _{1/2} (min)	156±43	137±17	148±28	196±60
Ranitidine				
AUC ₀₋₄₈₀ (µg.min/mL)	350±33	747±39 *	421±49	599±39 *
AUC _∞ (µg.min/mL)	570±165	948±71 *	526±65	703±61 *
c _{max} (µg/mL)	2±0.8	3±0.6 *	2±0.3	3±0.3 *
t _{max} (min)	116±90	168±50	117±78	123±37
CL (mL/min)	0.02±0.005	0.01±0.001	0.02±0.003	0.02±0.002
Vd (mL)	12±5	5±1 *	8±1	5±1
t _{1/2} (min)	407±37	288±70 *	231±54	193±51
Metformin				
AUC ₀₋₄₈₀ (µg.min/mL)	126±12	127±18	119±12	106±20
AUC _∞ (µg.min/mL)	130±12	136±18	129±14	147±29
c _{max} (µg/mL)	0.6±0.1	0.6±0.06	0.5±0.06	0.5±0.1
t _{max} (min)	98±25	105±46	135±59	138±58
CL (mL/min)	0.09±0.008	0.09±0.01	0.1±0.01	0.09±0.01
Vd (mL)	13±2	19±3	18±3	16±4
t _{1/2} (min)	100±15	142±16	129±18	150±39